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## PASSWORD:

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(FILE 'HOME' ENTERED AT 06:35:08 ON 05 JUN 2007)

FILE 'CAPLUS' ENTERED AT 06:36:30 ON 05 JUN 2007 L1 1 S US200!-510907/APPS

FILE 'REGISTRY' ENTERED AT 06:36:36 ON 05 JUN 2007

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FILE 'REGISTRY' ENTERED AT 06:36:39 ON 05 JUN 2007 L3 274 SEA L2

FILE 'REGISTRY' ENTERED AT 08:04:37 ON 05 JUN 2007

L4 STRUCTURE UPLOADED

L5 1 S L4

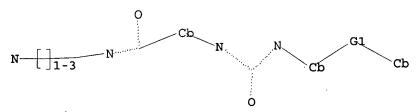
L6 66 S L4 SSS FULL

FILE 'CAPLUS' ENTERED AT 08:05:48 ON 05 JUN 2007 L7 6 S L6

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L4 HAS NO ANSWERS

L4 STR



G1 O, N

Structure attributes must be viewed using STN Express query preparation.

#### > d 17 tot bib abs hitstr

- L7 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2006:874421 CAPLUS <<LOGINID::20070605>>
- DN 145:376982
- TI Solid-phase synthesis and structure-activity relationships of novel biarylethers as melanin-concentrating hormone receptor-1 antagonists
- AU Ma, Vu; Bannon, Anthony W.; Baumgartner, Jamie; Hale, Clarence; Hsieh, Faye; Hulme, Christopher; Rorrer, Kirk; Salon, John; van Staden, Carlo; Tempest, Paul
- CS Chemistry Research and Discovery, Amgen Inc., Thousand Oaks, CA, 91320,
- SO Bioorganic & Medicinal Chemistry Letters (2006), 16(19), 5066-5072 CODEN: BMCLE8; ISSN: 0960-894X
- PB Elsevier Ltd.
- DT Journal
- LA English
- AB Melanin-concentrating hormone (MCH) is a cyclic 19 amino acid orexigenic neuropeptide. The action of MCH on feeding is thought to involve the activation of its resp. G protein-coupled receptor MCH-R1. Consequently, antagonists that block MCH regulated MCH-R1 activity may provide a viable approach to the treatment of diet-induced obesity. This communication reports the discovery of a novel MCH-R1 receptor antagonist, which was identified through high throughput screening. The solid-phase synthesis and structure-activity relationship of related analogs is described.
- IT 846020-68-6P
  - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
    - (solid phase synthesis and structure-activity relationships of biarylethers as melanin-concentrating hormone receptor-1 antagonists identified through high throughput screening)
- RN 846020-68-6 CAPLUS
- CN Benzamide, 4-(3,4-dimethylphenoxy)-3-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



## RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:315070 CAPLUS <<LOGINID::20070605>>

DN 145:285

TI Identification of 4-amino-2-cyclohexylaminoquinazolines as metabolically stable melanin-concentrating hormone receptor 1 antagonists

AU Kanuma, Kosuke; Omodera, Katsunori; Nishiguchi, Mariko; Funakoshi, Takeo; Chaki, Shigeyuki; Nagase, Yasuko; Iida, Izumi; Yamaguchi, Jun-ichi; Semple, Graeme; Tran, Thuy-Anh; Sekiguchi, Yoshinori

CS Medicinal Research Laboratories, Taisho Pharmaceutical Co. Ltd, Saitama, Saitama, 331-9530, Japan

SO Bioorganic & Medicinal Chemistry (2006), 14(10), 3307-3319 CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier B.V.

DT Journal

LA English

The optimization of the distance between two key pharmacophore features within our first hit compds. led to the identification of a new class of potent non-peptidic antagonists for the MCH-R1, based around 4-amino-2-cyclohexylaminoquinazolines. In particular, ATC0065, N 2-[cis-4-({2-[4-Bromo-2-(trifluoromethoxy)phenyl]ethyl}amino)cyclohexyl]-N4,N4-dimethylquinazoline-2,4-diamine dihydrochloride, bound with high affinity to the MCH-R1 (IC50 value of 16 nM) and showed good metabolic stability in liver microsomes from human and rat.

IT 617245-27-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino cyclohexylaminoquinazolines as metabolically stable melanin-concentrating hormone receptor 1 antagonists)

RN 617245-27-9 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ & \\ & & \\ &$$

# RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L7 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2005:182684 CAPLUS <<LOGINID::20070605>>
- DN 142:254663
- TI Amine-containing phenyl derivative melanin-concentrating hormone receptor antagonists for therapeutic use

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Amgen, Inc., USA
SO
     PCT Int. Appl., 319 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                                             APPLICATION NO.
                          KIND
                                 DATE
                                                                     DATE
                          _ _ _ _
ΡI
     WO 2005019240
                           A2
                                 20050303
                                             WO 2004-US25970
                                                                      20040811
     WO 2005019240
                           А3
                                 20050506
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     AU 2004266228
                                             AU 2004-266228
                           A2
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                                                                     20040811
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                           A1
                                 20050303
     CA 2534428
                           A1
                                 20050303
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                                             US 2004-916219
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     EP 1654225
                                 20060510
                                             EP 2004-780754
                           A2
                                                                     20040811
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
     JP 2007502283
                           Т
                                 20070208
                                             JP 2006-523322
                                                                     20040811
PRAI US 2003-494855P
                           Р
                                 20030813
     WO 2004-US25970
                                 20040811
                           W
os
     MARPAT 142:254663
GΙ
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Tempest, Paul; Hulme, Christopher; Ma, Vu

IN

PA

AΒ The title compds., or pharmaceutically-acceptable salts, tautomers or prodrugs thereof, are provided. Also provided are methods for treating or preventing a melanin-concentrating hormone-mediated disorder in a subject, comprising administering to a subject in need of such treatment or prevention a compound of the invention. Preparation of compds, e.g. I, is

Ι

described.

IT 846020-68-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amine-containing Ph derivative melanin-concentrating hormone receptor antagonists for

therapeutic use)

RN 846020-68-6 CAPLUS

CN Benzamide, 4-(3,4-dimethylphenoxy)-3-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A



- L7 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
- AN 2004:767279 CAPLUS <<LOGINID::20070605>>
- DN 141:405643
- TI 4-Acylamino-and 4-ureidobenzamides as melanin-concentrating hormone (MCH) receptor 1 antagonists
- AU Receveur, Jean-Marie; Bjurling, Emelie; Ulven, Trond; Little, Paul Brian; Norregaard, Pia K.; Hoegberg, Thomas
- CS 7TM Pharma A/S, Horsholm, DK-2970, Den.
- SO Bioorganic & Medicinal Chemistry Letters (2004), 14(20), 5075-5080 CODEN: BMCLE8; ISSN: 0960-894X
- PB Elsevier B.V.

DT Journal

LA English

OS CASREACT 141:405643

AB Synthesis, in vitro biol. evaluation and structure-activity relationships of 4-acylamino-and 4-ureidobenzamides as novel hMCH1R-antagonists are disclosed. The nature of the amine side chains could be varied considerably in contrast to the central benzamide scaffold and aromatic substituents.

TT 617244-46-9 617244-63-0 617245-16-6 617245-17-7 617245-26-8 617245-27-9 617245-56-4 617245-67-7 617246-05-6 617246-53-4 617246-60-3 791613-58-6 791613-65-5 791613-66-6 791613-67-7 791613-69-9

RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)

(4-Acylamino-and 4-ureidobenzamides as melanin-concentrating hormone (MCH) receptor 1 antagonists)

RN 617244-46-9 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-63-0 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-methoxy-4-[methyl[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OMe} \\ \text{Et}_2\text{N-CH}_2\text{-CH}_2\text{-NH-C} \\ \hline \\ \text{Me O} \\ \text{N-C-NH} \\ \end{array}$$

RN 617245-16-6 CAPLUS

CN Benzamide, 2-methoxy-4-[[[[4-(phenylamino)phenyl]amino]carbonyl]amino]-N[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 617245-17-7 CAPLUS

CN Benzamide, 2-methoxy-4-[[[[3-(phenylamino)phenyl]amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 617245-26-8 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 617245-27-9 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 617245-56-4 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(4-morpholinyl)propyl]-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-67-7 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-ethoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617246-05-6 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-methoxy-4-[[[methyl(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \mathsf{Et_2N-CH_2-CH_2-NH-C} & \mathsf{OMe} \\ \hline \\ \mathsf{NH-C-N} & \mathsf{OMe} \\ \hline \end{array}$$

RN 617246-53-4 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-4-[[[(4-phenoxyphenyl)amino]carbonyl] amino]- (9CI) (CA INDEX NAME)

RN 617246-60-3 CAPLUS

CN Benzamide, 4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

RN 791613-58-6 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(2-phenoxyphenyl)amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 791613-65-5 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-methoxy-4-[methyl[[methyl(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 791613-66-6 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-N-methyl-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 791613-67-7 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-methoxy-N-methyl-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

Pho OMe OMe 
$$\parallel \parallel \parallel$$
 C NH CH2 CH2 NEt2

RN 791613-69-9 CAPLUS

CN Benzamide, 5-chloro-N-[2-(diethylamino)ethyl]-2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:837035 CAPLUS <<LOGINID::20070605>>

DN 139:337787

TI Preparation of novel methoxybenzamides for use in MCH receptor related disorders

CODEN: PIXXD2

DT Patent LA English

FAN.CNT 2 APPLICATION NO. DATE PATENT NO. KIND DATE ----------PΙ WO 2003087045 A1\_ 20031023 WO 2003-DK231 20030408 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG 20030408 CA 2482341 **A1** 20031023 CA 2003-2482341 AU 2003226926 **A1** 20031027 AU 2003-226926 20030408 EP 1497260 **A1** 20050119 EP 2003-746255 20030408 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK 20061019 US 2005-510907 US 2006235035 Α1 20050516 PRAI DK 2002-519 20020409 Α DK 2002-520 20020409 Α DK 2002-524 Α 20020409 DK 2002-1818 Α 20021125 WO 2003-DK231 W 20030408 MARPAT 139:337787 os GI

$$\begin{array}{c|cccc}
R^{5} & & & & & \\
R^{5} & & & & & \\
R^{8} & & & & & \\
\end{array}$$

AB Title compds. I [wherein A = a linker, e.g. CHR7CONR7, CONR7, OCONR7, SO2NR7, CHR7NR7CO, NR7COR7, hexahydro-2-oxo-pyrimidine-1,3-diyl, 2-oxoimidazolidine-1,3-diyl, 1,2,4-oxadiazolediyl, 1,3,4-oxadiazolediyl, CH=CH, OCHR7, NR7CHR7, SCHR7, or (un)substituted imidazolediyl or 1,2,4-triazolediyl; Ar = independently (hetero)aryl; R1 = alkoxy; R2 = H, OH, NH2, or alkoxy; COQ = amino-substituted amide; R5 and R6 = independently H, halo, alkoxy, OH, (di)alkylamino, hydroxyalkyl,

II

I

carboxamido, acyl(amido), CHO, nitrile, alkyl, alkenyl, alkynyl, SMe,
 (fluoro)alkyl, (fluoro)alkoxy, (fluoro)thioalkoxy, SO2NH2,
 (di)alkylaminosulfonyl, or alkylsulfonyl; R7 = independently H, alkyl, or
 alkenyl; R8 = halo, (alkyl)(cyclo)alkyl, alkenyl, alkynyl,
 (alkyl)(hetero)aryl, (alkyl)heterocyclyl, (aryl)alkoxy, aryloxy,
 dialkylamino, (di)alkylcarbamoyl, (di)arylcarbamoyl, alkanoyl(amino),
 aroyl(amino), SMe, (fluoro)alkyl, (fluoro)alkoxy, (fluoro)thioalkoxy, or
 R6ArB; B = a single bond or connecting moiety; X = H, halo, SMe, CF3,
 OCF3, SCF3, OMe, alkyl, or alkenyl; and physiol. acceptable salts,
 complexes, solvates, and prodrugs thereof] were prepared as
melanin-concentrating

hormone (MCH) receptor modulators. For example, coupling of procainamide with 4-trifluoromethoxyphenyl isocyanate in the presence of TEA in CH2Cl2 gave II (59%). In assays of [125I]-MCH binding and phosphatidylinositol turnover using transiently transfected COS-7 cells or stably transfected CHO cells expressing the human MCH-1 receptor, II exhibited activity with IC50 values of 0.07  $\mu\text{M}$  and 0.29  $\mu\text{M}$ , resp. Administration of II (10 mg/kg i.p.) to male Sprague Dawley rats resulted in a significant reduction of their cumulative food intake over 6 h. Thus, I and their pharmaceutical compns. are useful in the treatment or prevention of obesity, depression, diabetes, bulimia, and other MCH receptor related disorders (no data).

IT 617245-28-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(MCH receptor modulator; preparation of methoxybenzamides as MCH receptor modulators for treatment of obesity, depression, diabetes, bulimia, and related disorders)

RN 617245-28-0 CAPLUS

related disorders)

CN Benzamide, 4-[[[[3-(4-fluorophenoxy)phenyl]amino]carbonyl]amino]-2-methoxy-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

ΙT 617244-39-0P 617244-42-5P 617244-43-6P 617244-44-7P 617244-45-8P 617244-46-9P 617244-48-1P 617244-52-7P 617244-53-8P 617244-54-9P 617244-55-0P 617244-56-1P 617244-58-3P 617244-63-0P 617245-16-6P 617245-17-7P 617245-18-8P 617245-20-2P 617245-22-4P 617245-24-6P 617245-25-7P 617245-26-8P 617245-27-9P 617245-29-1P · 617245-30-4P 617245-32-6P 617245-33-7P 617245-39-3P 617245-41-7P 617245-42-8P 617245-45-1P 617245-46-2P 617245-48-4P 617245-50-8P 617245-51-9P 617245-52-0P 617245-53-1P 617245-56-4P 617245-57-5P 617245-58-6P 617245-59-7P 617245-67-7P 617245-69-9P 617245-70-2P 617245-72-4P 617245-87-1P 617246-05-6P 617246-06-7P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (MCH receptor modulator; preparation of methoxybenzamides as MCH receptor

modulators for treatment of obesity, depression, diabetes, bulimia, and

RN 617244-39-0 CAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-42-5 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(4-methyl-1-piperazinyl)propyl]-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-43-6 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

RN 617244-44-7 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 617244-45-8 CAPLUS

CN Benzamide, 2-methoxy-N-[2-(4-morpholinyl)ethyl]-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-46-9 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-48-1 CAPLUS

CN Benzamide, N-[2-[bis(1-methylethyl)amino]ethyl]-2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-52-7 CAPLUS

CN Benzamide, N-[2-(diethylamino)-1-methylethyl]-2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-53-8 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

RN 617244-54-9 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(4-morpholinyl)propyl]-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-55-0 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(2-methyl-1-piperidinyl)propyl]-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-56-1 CAPLUS

CN Benzamide, N-[3-(diethylamino)propyl]-2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

PhO OME 
$$C-NH-(CH_2)_3-NEt_2$$

RN 617244-58-3 CAPLUS

CN Benzamide, N-[3-(dibutylamino)propyl]-2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617244-63-0 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-methoxy-4-[methyl[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-16-6 CAPLUS

CN Benzamide, 2-methoxy-4-[[[[4-(phenylamino)phenyl]amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 617245-17-7 CAPLUS

CN Benzamide, 2-methoxy-4-[[[[3-(phenylamino)phenyl]amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 617245-18-8 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(1-piperidinyl)propyl]-4-[[[[4-[[3-(trifluoromethoxy)phenyl]amino]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

$$-N$$

RN 617245-20-2 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(1-piperidinyl)propyl]-4-[[[[4-[4-(trifluoromethoxy)phenyl]amino]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

$$-$$
N

RN 617245-22-4 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(1-piperidinyl)propyl]-4-[[[[3-[[3-(trifluoromethoxy)phenyl]amino]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-B

$$-$$
N $\bigcirc$ 

RN 617245-24-6 CAPLUS

CN Benzamide, 2-methoxy-4-[[[[3-[(4-methoxyphenyl)amino]phenyl]amino]carbonyl amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 617245-25-7 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(1-piperidinyl)propyl]-4-[[[[3-[[4-(trifluoromethyl)phenyl]amino]phenyl]amino]carbonyl]amino]- (9CI) (CAINDEX NAME)

F<sub>3</sub>C OMe OMe 
$$C-NH-(CH_2)_3-N$$

RN 617245-26-8 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 617245-27-9 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ \text{PhO} & & \\ & & \\ \text{NH-C-NH-} & \\ & & \\ \text{OMe} & & \\ \end{array}$$

RN 617245-29-1 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(1-piperidinyl)propyl]-4-[[[[4-[4-(trifluoromethyl)phenoxy]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-30-4 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(1-piperidinyl)propyl]-4-[[[[4-[4-(trifluoromethoxy)phenoxy]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-32-6 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(1-piperidinyl)propyl]-4-[[[[3-[3-(trifluoromethyl)phenoxy]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 617245-33-7 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(1-piperidinyl)propyl]-4-[[[[4-[3-(trifluoromethoxy)phenoxy]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-39-3 CAPLUS

CN Benzamide, 2-methoxy-N-[2-(4-morpholinyl)ethyl]-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ &$$

RN 617245-41-7 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-42-8 CAPLUS

CN Benzamide, 2-methoxy-N-[3-[methyl(1-methylethyl)amino]propyl]-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-45-1 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 617245-46-2 CAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-48-4 CAPLUS

CN Benzamide, N-[3-(dimethylamino)-2,2-dimethylpropyl]-2-methoxy-4-[[[(3-

phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-50-8 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\$$

RN 617245-51-9 CAPLUS

CN Benzamide, N-[2-(diethylamino)-1-methylethyl]-2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-52-0 CAPLUS

CN Benzamide, N-[3-(dimethylamino)propyl]-2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OPh} & \text{OMe} & \text{O} \\ \hline \\ \text{O} & \text{C-NH-(CH2)}_3 - \text{NMe}_2 \\ \hline \\ \text{NH-C-NH-} \end{array}$$

RN 617245-53-1 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(4-methyl-1-piperazinyl)propyl]-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-56-4 CAPLUS

CN Benzamide, 2-methoxy-N-[3-(4-morpholinyl)propyl]-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-57-5 CAPLUS

CN Benzamide, 2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]-N-[4-(1-pyrrolidinyl)butyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



RN 617245-58-6 CAPLUS

CN Benzamide, N-[3-(diethylamino)propyl]-2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617245-59-7 CAPLUS

CN Benzamide, N-[4-(dimethylamino)butyl]-2-methoxy-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OPh} & \text{OMe} & \text{O} \\ \hline \\ \text{O} & \text{C-NH-} \text{(CH}_2)_4 - \text{NMe}_2 \\ \hline \\ \text{NH-C-NH-} \end{array}$$

RN 617245-67-7 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-ethoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

PhO OET 
$$C-NH-CH_2-CH_2-NEt_2$$

RN 617245-69-9 CAPLUS

CN Benzamide, N-[3-(dibutylamino)propyl]-2-methoxy-4-[methyl[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$(n-Bu)_2N-(CH_2)_3-NH-C$$

Me O

 $N-C-NH$ 

OPh

RN 617245-70-2 CAPLUS

CN Benzamide, 4-[[[[4-(4-fluorophenoxy)phenyl]amino]carbonyl]amino]-2-methoxy-N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

RN 617245-72-4 CAPLUS

RN 617245-87-1 CAPLUS

CN Benzamide, 2-methoxy-N-[3-[(1-methylethyl)(phenylmethyl)amino]propyl]-4-[[[(3-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617246-05-6 CAPLUS

CN Benzamide, N-[2-(diethylamino)ethyl]-2-methoxy-4-[[[methyl(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{C} & \text{OMe} \\ & \text{O} & \text{OMe} \\ \hline & \text{O} & \text{Me} \\ \hline & \text{NH-C-N} \end{array} \\ \end{array}$$

RN 617246-06-7 CAPLUS

CN Benzamide, 2-methoxy-4-[[[methyl(4-phenoxyphenyl)amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

PhO Me O 
$$C-NH-(CH_2)_3-N$$
 OMe

IT 617246-16-9P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of methoxybenzamides as MCH receptor modulators for treatment of obesity, depression, diabetes, bulimia, and related disorders)

RN617246-16-9 CAPLUS

CNBenzamide, 5-fluoro-2-methoxy-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[3-(1-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

#### RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

AN

DN 139:337786

Preparation of novel benzamides for use in MCH receptor related disorders TI

Ulven, Trond; Hoegberg, Thomas; Elling, Christian E.; Norregaard, Pia IN Karina; Bjurling, Anna Emelie; Receveur, Jean-Marie; Little, Paul Brian

PA 7TM Pharma A/S, Den.

SO PCT Int. Appl., 63 pp. CODEN: PIXXD2

DT Patent

English LA

FAN.CNT 1																		
	PA	PATENT NO.			KIND		DATE		APPLICATION NO.					DATE				
PΙ	MÓ	2003087044			A2		20031023		WO 2003-DK232				20030408					
	WO	2003087044			A:3	A3 20041104												
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			GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	OM,
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		•	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	ΒE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
			FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
			BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
	ΑU	J 2003226927			<b>A1</b>		2003	1027	AU 2003-226927				20030408					
PRAI	DK	2002	-518			Α		2002	0409									
	DK	2002	-757			Α		2002	0516									
	WO	2003	-DK2	32		W		2003	0408									

$$R^{6}$$
  $Ar^{2}$   $B$   $Ar^{1}$   $A$   $R^{2}$   $R^{2}$   $R^{2}$   $R^{2}$   $R^{2}$   $R^{2}$ 

ΔR Title compds. I [wherein A = a linker, e.g. CHR7CONR7, CONR7, OCONR7, SO2NR7, CHR7NR7CO, NR7CONR7, hexahydro-2-oxo-pyrimidine-1,3-diyl, 2-oxoimidazolidine-1,3-diyl, 1,2,4-oxadiazolediyl, 1,3,4-oxadiazolediyl, (un) substituted imidazolediyl or 1,2,4-triazolediyl, CH=CH, OCHR7, NR7CHR7, or SCHR7; B = CH2, OCH2, O, SO2, NR7, S, NR7CH2, SCH2, CONR7, SO2NR7, CO, or CHOR7; Ar1 and Ar2 = independently (hetero)aryl; R1 and R2 = independently H, halo, CF3, OCF3, SCF3, SMe, nitrile, alkyl, alkenyl, or alkynyl; or R1 and R2 may be connected to each other to form annelated rings; R5 and R6 = independently H, halo, alkoxy, OH, (di)alkylamino, hydroxyalkyl, carboxamido, acyl(amido), CHO, nitrile, alkyl, alkenyl, alkynyl, SMe, (fluoro)alkyl, (fluoro)alkoxy, (fluoro)thioalkoxy, SO2NH2, (di)alkylaminosulfonyl, or alkylsulfonyl; more than one R5 and/or R6 may be present; Q = substituted amino; R7 = independently H, alkyl, or alkenyl; n = 1-3; and physiol. acceptable salts, complexes, solvates, and prodrugs thereof] were prepared as melanin-concentrating hormone (MCH) receptor modulators. For example, coupling of 4-aminobenzoic acid with 4-phenoxyphenyl isocyanate in DCM gave 4-[3-(4phenoxyphenyl)ureido]benzoic acid (79%). Condensation of the acid with 2-(aminomethyl)-1-ethylpyrrolidine afforded the ureidobenzamide II (34%). In assays of [1251]-MCH binding and phosphatidylinositol turnover using transiently transfected COS-7 cells or stably transfected CHO cells. expressing the human MCH-1 receptor, II exhibited activity with IC50 values of 0.25  $\mu M$  and 1.3  $\mu M,$  resp. Thus, I and their pharmaceutical compns. are useful in the treatment or prevention of obesity, depression, diabetes, bulimia, and other MCH receptor related disorders (no data).

IT 617246-49-8P 617246-50-1P 617246-51-2P 617246-52-3P 617246-53-4P 617246-56-7P 617246-59-0P 617246-60-3P 617246-61-4P 617246-62-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(MCH receptor modulator; preparation of benzamides as MCH receptor modulators for treatment of obesity, depression, diabetes, bulimia, and related disorders)

RN 617246-49-8 CAPLUS

CN Benzamide, N-[3-(dimethylamino)propyl]-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$Me_{2}N-(CH_{2})_{3}-NH-C$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

RN 617246-50-1 CAPLUS

CN Benzamide, 4-[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

RN 617246-51-2 CAPLUS

CN Benzamide, N-[2-(4-morpholinyl)ethyl]-4-[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617246-52-3 CAPLUS

CN Benzamide, 4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 2-A

617246-53-4 CAPLUS RN

Benzamide, N-[2-(diethylamino)ethyl]-4-[[[(4-phenoxyphenyl)amino]carbonyl] CNamino] - (9CI) (CA INDEX NAME)

RN

617246-56-7 CAPLUS Benzamide, N-[2-(dimethylamino)ethyl]-4-[[[(4-CNphenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & & & & \\ & & & & & & & \\ \text{Me}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{C} & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ \end{array}$$

RN 617246-59-0 CAPLUS

CN Benzamide, N-[2-[bis(1-methylethyl)amino]ethyl]-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 617246-60-3 CAPLUS

CN Benzamide, 4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 617246-61-4 CAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-N-methyl-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O \\ \hline \\ PhO \\ \hline \\ \hline \\ C-N-CH_2-CH_2-NMe_2 \\ \hline \\ O Me \\ \end{array}$$

RN 617246-62-5 CAPLUS

CN Benzamide, N-methyl-N-[3-(4-methyl-1-piperazinyl)propyl]-4-[[[(4-phenoxyphenyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

Me O NH-C-NH

N- (CH<sub>2</sub>) 
$$_3$$
 - N- C

OPh

=> log hold

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 32.09 223.47 TOTAL DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY SESSION CA SUBSCRIBER PRICE -4.68 -4.68

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:06:14 ON 05 JUN 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptasjl1626

### PASSWORD:

\* \* \* \* \* \* RECONNECTED TO STN INTERNATIONAL \* \* \* \* \* \* SESSION RESUMED IN FILE 'CAPLUS' AT 08:06:30 ON 05 JUN 2007 FILE 'CAPLUS' ENTERED AT 08:06:30 ON 05 JUN 2007 COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	. ENTRY 32.09	SESSION 223.47
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY -4.68	SESSION -4.68

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L4

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FILE 'REGISTRY' ENTERED AT 06:36:36 ON 05 JUN 2007

FILE 'CAPLUS' ENTERED AT 06:36:39 ON 05 JUN 2007 L2 TRA L1 1- RN : 274 TERMS

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FILE 'CAPLUS' ENTERED AT 08:05:48 ON 05 JUN 2007

L7 6 S L6

=> d 14

L4 HAS NO ANSWERS

L4 STR

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Structure attributes must be viewed using STN Express query preparation.

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SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:06:53 ON 05 JUN 2007

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	FILE	'STNGUIDE' ENTERED AT 11:35:27 ON 05 JUN 2007
L5 L6	FILE	'CAPLUS' ENTERED AT 11:35:56 ON 05 JUN 2007 1 S US7067506/PN 2 S L4 OR L5
	FILE	'REGISTRY' ENTERED AT 11:37:12 ON 05 JUN 2007
L7	FILE	'CAPLUS' ENTERED AT 11:37:16 ON 05 JUN 2007 TRA L6 1- RN : 1000 TERMS
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•	FILE	'STNGUIDE' ENTERED AT 11:37:25 ON 05 JUN 2007
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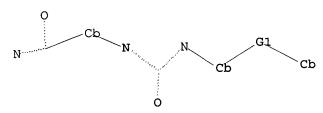
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Structure attributes must be viewed using STN Express query preparation.

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Structure attributes must be viewed using STN Express query preparation.

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ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
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DN
     137:232680
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     Preparation of aryl and heteroaryl urea selective Chk1 inhibitors for use
     as radiosensitizers and chemosensitizers for treating diseases and
     conditions related to DNA damage or lesions in DNA replication
     Keegan, Kathleen S.; Kesicki, Edward A.; Gaudino, John Joseph; Cook, Adam
IN
     Wade; Cowen, Scott Douglas; Burgess, Laurence Edward
     Icos Corporation, USA
PA
SO
     PCT Int. Appl., 236 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
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                                                                  DATE
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                                                                  20020301
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     WO 2002-US6452
                        W
                               20020301
     MARPAT 137:232680
OS
AB
    Aryl- and heteroaryl substituted urea compds. (W'NHC(:Y')N(R13)Z'; 1)
     useful in the treatment of diseases and conditions related to DNA damage
     or lesions in DNA replication are disclosed. In 1, W' is a six-membered
     aromatic ring containing at least 2 nitrogen atoms (e.g. pyrazinyl,
pyrimidinyl,
     pyridazinyl, 1,2,4-triazinyl, quinoxalinyl) and optionally substituted as
     defined in the claims, Z' is a five- or six membered aromatic or heteroarom.
     ring as defined in the claims, Y' is O or S. The first claim contains a
     much more general formula WX1C(:Y)X2Z (e.g. X1 = null, O, S, CH2, NR1; X2
     = 0, S, NR1) but emphasis is on 1. Methods of making the compds., and
     their use as therapeutic agents, for example, in treating cancer and other
     diseases characterized by defects in DNA replication, chromosome
     segregation, or cell division also are described. Although the methods of
     preparation are not claimed, about 200 example prepns. are included.
    N-(2-methoxy-5-methylphenyl)-N'-(2-pyrazinyl)urea and N-(4-chloro-2-
    methoxyphenyl)-N'-(2-pyrazinyl)urea enhanced the killing of various human
     cells by 5-fluorouracil from 2- to 10-fold; in HeLa cells, these same
```

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compds. enhanced killing by irradiation 2-3 fold.
     457097-05-1P, 3-Methoxy-N-[3-(methylphenylamino)propyl]-4-(3-
     (pyrazin-2-yl) ureido) benzamide 457097-16-4P,
     N-(2-Dimethylaminoethyl)-3-methoxy-N-methyl-4-(3-(pyrazin-2-
     yl)ureido)benzamide 457097-18-6P, 3-Methoxy-N-(3-
     methylaminopropyl)-4-(3-(pyrazin-2-yl)ureido)benzamide 457097-21-1P**
        , N-(3-Dimethylaminopropyl)-3-methoxy-4-(3-(pyrazin-2-
     yl)ureido)benzamide ***457097-23-3P, N-(3-Dimethylaminopropyl)-3-
     methoxy-N-methyl-4-(3-(pyrazin-2-yl)ureido)benzamide 457097-25-5P
     , 3-Methoxy-N-(3-(morpholin-4-yl)propyl)-4-(3-(pyrazin-2-yl)propyl)
     yl)ureido)benzamide 457097-27-7P, 3-Methoxy-N-[3-(4-
     methylpiperazin-1-yl)propyl]-4-(3-(pyrazin-2-yl)ureido)benzamide
     457097-29-9P, [2-[3-Methoxy-4-(3-(pyrazin-2-
     yl)ureido)benzoylamino]ethyl]trimethylammonium chloride
     457097-44-8P, 4-Methoxy-N-[3-(methylphenylamino)propyl]-3-(3-
     (pyrazin-2-yl)ureido)benzamide 457097-46-0P,
     N-(2-Dimethylaminoethyl)-4-methoxy-N-methyl-3-(3-(pyrazin-2-
     yl)ureido)benzamide 457097-47-1P, 4-Methoxy-N-(3-
     methylaminopropyl) -3-(3-(pyrazin-2-yl) ureido) benzamide
     457097-48-2P, N-(3-Dimethylaminopropyl)-4-methoxy-3-(3-(pyrazin-2-
     yl)ureido)benzamide 457097-49-3P, N-(3-Dimethylaminopropyl)-4-
     methoxy-N-methyl-3-(3-(pyrazin-2-yl)ureido)benzamide 457097-50-6P
     , 4-Methoxy-N-[3-(4-methylpiperazin-1-yl)propyl]-3-(3-(pyrazin-2-
     yl)ureido)benzamide 457097-51-7P, [2-[4-Methoxy-3-(3-(pyrazin-2-
     yl)ureido)benzoylamino]ethyl]trimethylammonium chloride
     457097-52-8P, 4-Methoxy-N-(3-(morpholin-4-yl)propyl)-3-(3-(pyrazin-
     2-yl)ureido)benzamide 457097-61-9P, N-(3-Dimethylaminopropyl)-3-
     methoxy-4-[3-(5-methylpyrazin-2-yl)ureido]benzamide 457097-63-1P
       3-Methoxy-4-[3-(5-methylpyrazin-2-yl)ureido]-N-(3-(morpholin-4-
     yl)propyl)benzamide 457097-65-3P, N-(2-(Dimethylamino)-2-
     phenylethyl) -3-methoxy-4-[3-(5-methylpyrazin-2-yl)ureido]benzamide
     457097-68-6P, N-(2-(Dimethylamino)-1-phenylethyl)-3-methoxy-4-[3-
     (5-methylpyrazin-2-yl)ureido]benzamide 457098-25-8P,
     3-(3-Dimethylaminopropoxy)-4-[3-(5-methylpyrazin-2-yl)ureido]-N-(2-
     (morpholin-4-yl)ethyl)benzamide 457098-27-0P,
     N-(2-Dimethylaminoethyl)-3-(3-dimethylaminopropoxy)-4-[3-(5-methylpyrazin-
     2-yl)ureido]benzamide 457098-34-9P, 4-[3-(5-Methylpyrazin-2-
     yl)ureido] -N-(2-(morpholin-4-yl)ethyl)-3-(pyridin-3-ylmethoxy)benzamide
     457098-36-1P, N-(2-Dimethylaminoethyl)-4-[3-(5-methylpyrazin-2-
     yl)ureido]-3-(pyridin-3-ylmethoxy)benzamide 457099-93-3P,
     N-(2-Methoxy-3-((2-(4-morpholinyl)ethyl)carbamoyl)phenyl)-N'-(2-
     pyrazinyl)urea 457099-96-6P, N-(2-Methoxy-4-((2-(4-
     morpholinyl)ethyl)carbamoyl)phenyl)-N'-(2-pyrazinyl)urea
     457099-98-8P, N-(2-Methoxy-4-((2-((methylsulfonyl)amino)ethyl)carb
     amoyl)phenyl)-N'-(2-pyrazinyl)urea
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of aryl and heteroaryl urea selective Chk1 inhibitors for use
        as radiosensitizers and chemosensitizers for treating diseases and
        conditions related to DNA damage or lesions in DNA replication)
RN
     457097-05-1 CAPLUS
CN
     Benzamide, 3-methoxy-N-[3-(methylphenylamino)propyl]-4-
     [[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)
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RN 457097-16-4 CAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-3-methoxy-N-methyl-4-[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 457097-18-6 CAPLUS

CN Benzamide, 3-methoxy-N-[3-(methylamino)propyl]-4[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 457097-21-1 CAPLUS

CN Benzamide, N-[3-(dimethylamino)propyl]-3-methoxy-4[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O \\ | \\ C-NH-(CH_2)_3-NMe_2 \\ \hline \\ NM-C-NH-C-NH-(CH_2)_3-NMe_2 \\ \hline \\ OMe \end{array}$$

RN 457097-23-3 CAPLUS

CN Benzamide, N-[3-(dimethylamino)propyl]-3-methoxy-N-methyl-4-[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 457097-25-5 CAPLUS

CN Benzamide, 3-methoxy-N-[3-(4-morpholinyl)propyl]-4[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
O & O \\
O & N \\
O &$$

RN 457097-27-7 CAPLUS

CN Benzamide, 3-methoxy-N-[3-(4-methyl-1-piperazinyl)propyl]-4-[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{OMe} & \text{O} \\ & \text{N} & \text{NH-C-NH-N} \\ & \text{N} & \text{NH-C-NH-N} \\ & \text{N} & \text{NH-C-NH-N} \\ & \text{NH-C-$$

RN 457097-29-9 CAPLUS

CN Ethanaminium, 2-[[3-methoxy-4-[[(pyrazinylamino)carbonyl]amino]benzoyl]amino]-N,N,N-trimethyl-, chloride (9CI) (CA INDEX NAME)

• c1 ·

RN 457097-44-8 CAPLUS

CN Benzamide, 4-methoxy-N-[3-(methylphenylamino)propyl]-3[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 457097-46-0 CAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-4-methoxy-N-methyl-3-[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 457097-47-1 CAPLUS

CN Benzamide, 4-methoxy-N-[3-(methylamino)propyl]-3[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

RN 457097-48-2 CAPLUS

CN

Benzamide, N-[3-(dimethylamino)propyl]-4-methoxy-3-[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

RN 457097-49-3 CAPLUS

CN Benzamide, N-[3-(dimethylamino)propyl]-4-methoxy-N-methyl-3-[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 457097-50-6 CAPLUS

CN Benzamide, 4-methoxy-N-[3-(4-methyl-1-piperazinyl)propyl]-3[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 457097-51-7 CAPLUS

CN Ethanaminium, 2-[[4-methoxy-3-[[(pyrazinylamino)carbonyl]amino]benzoyl]amino]-N,N,N-trimethyl-, chloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & &$$

● c1 -

RN 457097-52-8 CAPLUS

CN Benzamide, 4-methoxy-N-[3-(4-morpholinyl)propyl]-3[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

RN 457097-61-9 CAPLUS

CN Benzamide, N-[3-(dimethylamino)propyl]-3-methoxy-4-[[[(5-methylpyrazinyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O \\
 & | \\
 & C-NH-(CH_2)_3-NMe_2 \\
\hline
 & N \\
 & N \\
 & OMe
\end{array}$$

RN 457097-63-1 CAPLUS

CN Benzamide, 3-methoxy-4-[[[(5-methylpyrazinyl)amino]carbonyl]amino]-N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

RN 457097-65-3 CAPLUS

CN Benzamide, N-[2-(dimethylamino)-2-phenylethyl]-3-methoxy-4-[[[(5-methylpyrazinyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

RN 457097-68-6 CAPLUS

CN Benzamide, N-[2-(dimethylamino)-1-phenylethyl]-3-methoxy-4-[[[(5-methylpyrazinyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\$$

RN 457098-25-8 CAPLUS

CN Benzamide, 3-[3-(dimethylamino)propoxy]-4-[[[(5-methylpyrazinyl)amino]carbonyl]amino]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 457098-27-0 CAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-3-[3-(dimethylamino)propoxy]-4-[[[(5-methylpyrazinyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

Me 
$$N + C + NH + C +$$

RN 457098-34-9 CAPLUS

CN Benzamide, 4-[[[(5-methylpyrazinyl)amino]carbonyl]amino]-N-[2-(4-morpholinyl)ethyl]-3-(3-pyridinylmethoxy)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 457098-36-1 CAPLUS

CN Benzamide, N-[2-(dimethylamino)ethyl]-4-[[[(5-methylpyrazinyl)amino]carbonyl]amino]-3-(3-pyridinylmethoxy)- (9CI) (CA INDEX NAME)

RN 457099-93-3 CAPLUS

CN Benzamide, 2-methoxy-N-[2-(4-morpholinyl)ethyl]-3[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & OMe \\ \hline O & N \\ \hline O & N$$

RN 457099-96-6 CAPLUS

CN Benzamide, 3-methoxy-N-[2-(4-morpholinyl)ethyl]-4[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O \\ O \\ N \\ O \\ O \\ \end{array}$$

$$\begin{array}{c|c} O \\ N \\ C \\ \end{array}$$

$$\begin{array}{c|c} O \\ N \\ \end{array}$$

RN 457099-98-8 CAPLUS

CN Benzamide, 3-methoxy-N-[2-[(methylsulfonyl)amino]ethyl]-4-[[(pyrazinylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT